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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/840,146	04/24/2001	Harlan W. Waksal	11245/46604	5311

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EXAMINER

HOLLERAN, ANNE L

ART UNIT PAPER NUMBER

1642

DATE MAILED: 12/17/2002

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Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b> 09/840,146	<b>Applicant(s)</b> WAKSAL, HARLAN W.	
	<b>Examiner</b> Anne Holleran	<b>Art Unit</b> 1642	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1) ☒ Responsive to communication(s) filed on August 22, 2002.

2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4) ☒ Claim(s) 36-127 is/are pending in the application.

4a) Of the above claim(s) 59-72 and 77-125 is/are withdrawn from consideration.

5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.

6) ☐ Claim(s) 36-58, 73-76, 126 and 127 is/are rejected.

7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.

8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All   b) ☐ Some \*   c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.

2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.

3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.	4) <input checked="" type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____. 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) 6) <input type="checkbox"/> Other: _____
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**DETAILED ACTION**

1. The election of group I in paper No. 7, filed August 21, 2002 is acknowledged. Upon reconsideration, the restriction requirement of paper No. 6 is withdrawn, and restated as set forth below.

2. Claims 36-127 are pending.

***Election/Restrictions***

3. Restriction to one of the following inventions is required under 35 U.S.C. 121:

- I. Claims 36-76, 126 and 127, drawn to methods for treatment comprising administering an EGFR antagonist and a chemotherapeutic agent, classified in class 424, subclass 130.1.
- II. Claims 77-125, drawn to methods for treatment comprising administering an EGFR antagonist and further treating with radiation therapy, classified in class 514, subclass 2.

4. The inventions are distinct, each from the other, for the following reasons:

Groups I and II are drawn to separate and distinct processes. The method of Group I is drawn to methods comprising coadministration of an EGFR antagonist and a chemotherapeutic agent. The method of Group II is drawn to methods of comprising administration of an EGFR antagonis and radiation, and also, in some cases, the coadministration of a chemotherapeutic

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agent. These methods are distinct because they employ different steps and therefore different search considerations. The methods of group II require the use of radiation therapy, whereas the methods of group I do not. Further, it would place an undue burden on the examiner to examine several, independent inventions in one application.

5. Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, restriction for examination purposes as indicated is proper.

6. Additionally, claims 36-52, 73-97, and 118-125 are generic to a plurality of disclosed patentably distinct species comprising EGFR antagonist. Applicant is required under 35 U.S.C. 121 to elect a single disclosed species, even though this requirement is traversed.

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

7. During a telephone conversation with Kathryn Lumb on October 25, 2002 a provisional election was made with traverse to prosecute the invention of group I, with election of species of EGFR antagonist to be an antibody. Affirmation of this election must be made by applicant in

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replying to this Office action. Claims 77-125 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

8. Applicant is advised that the reply to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.143).

9. Claims 36-58, 73-76, 126 and 127 are examined on the merits. Claims 59-72 do not read on the elected species and are withdrawn from consideration, because the elected species reads on the prior art.

10. Claims 48-50 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Factors to be considered in determining whether undue experimentation would be required to practice the full scope of the claimed inventions are: 1) quantity of experimentation necessary; 2) the amount of direction or guidance presented in the specification; 3) the presence or absence of working examples; 4) the nature of the invention; 5) the state of the prior art; 6) the relative skill of those in the art; 7) the predictability or unpredictability of the art; and 8) the breadth of the claims. See *Ex parte Forman*, 230 USPQ 546, BPAI, 1986.

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Claims 48-50 are drawn to methods comprising administering antibodies that bind the EGFR receptor, and bind EGFR internally, inhibiting binding of ATP to EGFR or compete with ATP for EGFR.

The specification lacks specific examples of methods comprising antibodies that act by this mechanism and lacks teachings for how to make and use such antibodies in the claimed methods. Because of the unpredictability in the art of therapy using antibodies, it appears that undue experimentation would be required to make and use the claimed inventions.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

11. Claims 36-47, and 51-53 are rejected under 35 U.S.C. 103(a) as being unpatentable over Baselga (J. Nat. Cancer Inst., 85: 1327-1333, 1993), Fan (Cancer Res., 53: 4637-4642, 1993) or

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Baselga (Breast Cancer Res. Treatment, 29: 127-138, 1994) in view of Mendelsohn (U.S. Patent 4,943,533; issued July, 1990).

Claims 36-47, and 51-53, 74 -76 are interpreted as drawn to methods of treatment comprising administering to a human an anti-EGFR antibody in combination with a chemotherapeutic agent. The claims may be limited by types of tumor, route of administration, dosage level, mechanism of inhibiting stimulation of EGFR by its ligand.

Any of Baselga (1993), Fan or Baselga (1994) teaches that the combination of EGFR antibody and chemotherapeutic agents such as doxorubicin, cisplatin or generally with chemotherapeutic agents is effective against cancer cells bearing the EGF receptor. Mendelsohn is discussed to demonstrate that the antibodies 225 and 528 are in the public domain and available for use.

Thus, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have developed a method for treatment of humans that comprised administering an antiEGF antibody and a chemotherapeutic agent. One would have had a reasonable expectation of success because of the teachings of Baselga (1994) that anti-EGF antibodies are tolerated well and have favorable pharmacokinetics.

12. Claims 36, 54-58 and 126 are rejected under 35 U.S.C. 103(a) as being unpatentable over Prewett and further in view of either Mateo de Acosta del Rio (U.S. Patent 5,891,996; issued Apr. 6, 1999; filing date Nov. 17, 1995) or Bendig (U.S. Patent 5,558,864; issued Sep. 24, 1996; filed Nov. 6, 1992).

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Claims 54-58, dependent from claim 36, and are drawn to methods where the anti-EGFR antibody is chimeric, humanized, human or administered at a dose to saturate EGFR. Claim 126 is drawn to a method for treatment comprising administering a chimeric anti-EGFR antibody and cisplatin.

Prewett teaches a method comprising a chimeric C225 antibody that binds EGFR in combination with cisplatin, where this combination is toxic to human xenograft tumors in nude mice. Mateo de Acosta del Rio and Bendig are discussed to demonstrate that methods for humanizing anti-EGFR antibodies are known in the art.

Thus, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have developed a method for treatment of humans that comprised administering chimeric, humanized or human antibodies and a chemotherapeutic agent. One would have had a reasonable expectation of success because the methods for humanizing and chimerizing antibodies is known in the art.

13. Claims 36, 74 and 127 are rejected under 35 U.S.C. 103(a) as being unpatentable over Baselga (Breast Cancer Res. Treatment, 29: 127-138, 1994) in combination with Prewett and further in view of Punt (Punt, Cancer, 83: 679-689, 1998).

Claims 36, 74 and 127 are interpreted as drawn to methods where the chemotherapeutic agent is irinotecan (CPT-11).

Baselga and Prewett fail to teach or suggest use of irinotecan in combination with an anti-EGFR antibody. However, Baselga teaches the general concept of combining antibody therapy with chemotherapeutic agents.



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Punt teaches that irinotecan is a new chemotherapeutic agent that is useful in the treatment of colorectal cancer. Thus, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have developed a method of treatment using anti-EGFR antibodies or chimeric anti-EGFR antibodies in combination with irinotecan for the treatment of colorectal cancer.

***Conclusion***


No claim is allowed.

Any inquiry concerning this communication or earlier communications from the Office should be directed to Anne Holleran, Ph.D. whose telephone number is (703) 308-8892. Examiner Holleran can normally be reached Monday through Friday, 9:30 am to 2:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, Ph.D. can be reached at (703) 308-3995.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist at telephone number (703) 308-0196.

Anne L. Holleran  
Patent Examiner  
December 16, 2002

  
ANTHONY G. CAPUTA  
SUPERVISOR, EXAMINER  
DEC 16 2002